

**Listing of Claims:**

Claims 1-37 (cancelled).

38. (previously presented) A method of inhibiting cartilage degradation in a joint of a patient, comprising:

delivering to the joint a composition in solution comprising a therapeutically effective amount of a first chondroprotective agent and a therapeutically effective amount of a second chondroprotective agent, wherein the first chondroprotective agent is an anabolic chondroprotective agent and the second chondroprotective agent is an inhibitor of cartilage catabolism, and the solution is delivered locally to the joint.

39. (previously presented) The method of Claim 38, wherein the solution is delivered to the joint by intra-articular injection.

40. (withdrawn) The method of Claim 39, wherein the solution comprises a sustained release delivery vehicle.

41. (withdrawn) The method of Claim 40, wherein the sustained release delivery vehicle is selected from the group consisting of microparticles, microspheres, nanoparticles, proteins, liposomes, carbohydrates, synthetic organic compounds and inorganic compounds.

42. (withdrawn) The method of Claim 38, wherein the solution is delivered to the joint by infusion.

43. (withdrawn) The method of Claim 42, wherein the solution is delivered to the joint by a regulated pump delivery system.

44. (previously presented) The method of Claim 38, wherein the solution is delivered to the joint for the treatment of a chronic cartilage degenerative condition.

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45. (previously presented) The method of Claim 38, wherein the solution is delivered to the joint prior to anticipated tissue trauma at the joint.

46. (previously presented) The method of Claim 38, wherein the solution is delivered to the joint at or closely following a time of injury to the joint.

47. (previously presented) The method of Claim 38, wherein the solution is delivered to the joint within a sub-acute phase following trauma to the joint.

48. (previously presented) The method of Claim 38, wherein the solution is delivered to the joint within a chronic phase following trauma to the joint.

49. (previously presented) The method of Claim 38, wherein the solution is locally applied prophylactically to the joint of a patient.

50. (previously presented) The method of Claim 38, further comprising the step of identifying a patient at risk of cartilage degradation at a joint, followed by delivering the solution to the joint of the identified patient.

51. (previously presented) The method of Claim 38, wherein each of the agents in the solution is included at a concentration or dosage that is sufficient to provide a level of inhibitory or therapeutic effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory or therapeutic effect at the wound when delivered systemically.

52. (previously presented) The method of Claim 38, wherein the anabolic chondroprotective agent is selected from the group consisting of interleukin (IL) agonists that promote cartilage anabolic processes, members of the transforming growth factor- $\beta$  superfamily, including TGF- $\beta$  agonists and bone morphogenic protein agonists, that promote

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cartilage anabolic processes, insulin-like growth factors that promote cartilage anabolic processes and fibroblast growth factors that promote cartilage anabolic processes.

53. (previously presented) The method of Claim 52, wherein the anabolic chondroprotective agent is selected from the group consisting of IL-4, IL-10, IL-13, TGF $\beta$ 1, TGF $\beta$ 2, TGF $\beta$ 3 BMP-2, BMP-4, BMP-6, BMP-7, IGF-1, bFGF and fragments, deletions, additions, amino acid substitutes, mutations and modifications that retain the biological characteristics of the naturally occurring agents.

54. (previously presented) The method of Claim 38, wherein the inhibitor of cartilage catabolism is selected from the group consisting of IL-1 receptor antagonists that inhibit cartilage catabolism, TNF- $\alpha$  receptor antagonists that inhibit cartilage catabolism, cyclooxygenase-2 specific inhibitors that inhibit cartilage catabolism, MAP kinase inhibitors that inhibit cartilage catabolism, nitric oxide synthase inhibitors that inhibit cartilage catabolism, and nuclear factor kB inhibitors that inhibit cartilage catabolism.

55. (withdrawn) The method of Claim 38, wherein the inhibitor of cartilage catabolism is selected from the group consisting of inhibitors of matrix metalloproteinases that inhibit cartilage catabolism, cell adhesion molecules, including integrin agonists and integrin antagonists, that inhibit cartilage catabolism, anti-chemotactic agents that inhibit cartilage catabolism, intracellular signaling inhibitors, including protein kinase C inhibitors and protein tyrosine kinase inhibitors, that inhibit cartilage catabolism, modulators of intracellular protein tyrosine phosphatases that inhibit cartilage catabolism, and inhibitors of SH2 domains that inhibit cartilage catabolism.

56. (withdrawn) The method of Claim 38, wherein the inhibitor of cartilage catabolism comprises a soluble receptor that inhibits cartilage catabolism.

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57. (withdrawn) The method of Claim 56, wherein the soluble receptor is selected from the group consisting of soluble interleukin-1 receptors and soluble tumor necrosis factor receptors.

58. (withdrawn) The method of Claim 56, wherein the soluble receptor is selected from the group consisting of recombinant soluble human IL-1 receptors, soluble tumor necrosis factor receptors and chimeric rhTNFR:Fc.

59. (withdrawn) The method of Claim 38, wherein the solution further comprises one or more pain or inflammation inhibitory agents.

60. (previously presented) The method of Claim 59, wherein the pain or inflammation inhibitory agents are selected from the group consisting of serotonin receptor antagonists, serotonin receptor agonists, histamine receptor antagonists, bradykinin receptor antagonists, kallikrein inhibitors, tachykinin receptor antagonists, calcitonin gene-related peptide (CGRP) receptor antagonists, interleukin receptor antagonists, inhibitors of enzymes active in the synthetic pathway for arachidonic acid metabolites, prostanoid receptor antagonists, leukotriene receptor antagonists, opioid receptor agonists, purinoceptor agonists and antagonists, adenosine triphosphate (ATP)-sensitive potassium channel openers, and calcium channel antagonists.

61. (withdrawn) A method of inhibiting cartilage degradation in a joint of a patient, comprising:

delivering to the joint a composition in solution comprising a therapeutically effective amount of a first chondroprotective agent and a therapeutically effective amount of a second chondroprotective agent, wherein the first chondroprotective agent is an anabolic chondroprotective agent and the second chondroprotective agent is an inhibitor of cartilage catabolism, and the solution is delivered locally and perioperatively to the joint during a surgical procedure.

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62. (withdrawn) The method of Claim 61, wherein the perioperative delivery of the solution comprises intraprocedural delivery together with preprocedural or postprocedural delivery of the solution.

63. (withdrawn) The method of Claim 61, wherein the perioperative application of the solution comprises preprocedural, intraprocedural and postprocedural application of the solution.

64. (withdrawn) The method of Claim 61, wherein each of the agents in the solution is included at a concentration or dosage that is sufficient to provide a level of inhibitory or therapeutic effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory or therapeutic effect at the wound when delivered systemically.

65. (withdrawn) A method of inhibiting cartilage degradation in a joint of a patient, comprising:

delivering to the joint a composition in solution comprising a therapeutically effective amount of a first chondroprotective agent and a therapeutically effective amount of a second chondroprotective agent, wherein the first chondroprotective agent is an anabolic chondroprotective agent and the second chondroprotective agent is an inhibitor of cartilage catabolism, and the solution is delivered locally to the joint by irrigating the joint with the solution during a surgical procedure.

66. (withdrawn) The method of Claim 65, wherein the procedure is an arthroscopic surgical procedure and the solution is delivered to the joint prior to, during or after the surgical procedure.

67. (withdrawn) The method of Claim 66, wherein the procedure is an arthroscopic surgical procedure and the solution is delivered to the joint prior to and during the surgical procedure.

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68. (withdrawn) The method of Claim 66, wherein the procedure is an arthroscopic surgical procedure and the solution is delivered to the joint prior to and after the surgical procedure.

69. (withdrawn) The method of Claim 66, wherein the procedure is an arthroscopic surgical procedure and the solution is delivered to the joint during and after the surgical procedure.

70. (withdrawn) The method of Claim 66, wherein a sufficient amount of the solution is delivered to the joint after the surgical procedure so that a bolus of the solution remains in the joint of the patient following the surgical procedure.

71. (withdrawn) The method of Claim 65, wherein the procedure is an arthroscopic surgical procedure and the solution is delivered to the joint prior to, during and after the surgical procedure.

72. (withdrawn) The method of Claim 65, wherein each of the agents in the solution is included at a concentration or dosage that is sufficient to provide a level of inhibitory or therapeutic effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory or therapeutic effect at the wound when delivered systemically.

73. (previously presented) A method of inhibiting cartilage degradation in a joint of a patient, comprising:

delivering to the joint a composition in solution comprising a therapeutically effective amount of a first chondroprotective agent and a therapeutically effective amount of a second chondroprotective agent, wherein the first chondroprotective agent is an anabolic chondroprotective agent and the second chondroprotective agent is an inhibitor of cartilage catabolism, the solution is delivered locally to the joint, and the solution is delivered to the joint within an acute phase following trauma to the joint.

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74. (previously presented) The method of Claim 73, wherein the solution is delivered during an acute phase following surgery.

75. (previously presented) The method of Claim 73, wherein the solution is delivered to the joint within a four week period following trauma to the joint.

76. (previously presented) The method of Claim 73, wherein the solution is delivered to the joint by intra-articular injection.

77. (withdrawn) The method of Claim 73, wherein the solution comprises a sustained release delivery vehicle.

78. (withdrawn) The method of Claim 77, wherein the sustained release delivery vehicle is selected from the group consisting of microparticles, microspheres, nanoparticles, proteins, liposomes, carbohydrates, synthetic organic compounds and inorganic compounds.

79. (withdrawn) The method of Claim 73, wherein the solution is delivered to the joint by infusion.

80. (withdrawn) The method of Claim 79, wherein the solution is delivered to the joint by a regulated pump delivery system.

81. (previously presented) The method of Claim 73, wherein each of the agents in the solution is included at a concentration or dosage that is sufficient to provide a level of inhibitory or therapeutic effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory or therapeutic effect at the wound when delivered systemically.

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